UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,305	10/12/2006	Takahide Nishi	06504/HG	5499

1933 7590 07/31/2007

FRISHAUF, HOLTZ, GOODMAN & CHICK, PC
220 Fifth Avenue
16TH Floor
NEW YORK, NY 10001-7708

EXAMINER	
AULAKH, CHARANJIT	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
07/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,305	NISHI ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,21,22,24-29 and 37-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,24-29 and 37-43* is/are rejected.

7)☒ Claim(s) *21,22 and 44-72* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/18/06, 11/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. According to a preliminary amendment filed on Aug. 23, 2006, the applicants have canceled claims 2-20, 23 and 30-36; amended claims 1, 21, 22, 24-29 and 37-43 and furthermore, have added new claims 44-72.

2. Claims 1, 21, 22, 24-29 and 37-72 are now pending in the application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 24-29 and 37-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:
Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation

necessary, the amount of direction or guidance provided, presence of working examples, state of the prior art, unpredictability and the breadth of claims.

In regard to lack of enablement issue of instant claim1 for derivatives (hydrates, solvates or prodrug forms) of instant compounds of formula (I), there is no teaching or guidance present in the specification for preparing any specific hydrates (mono, di, tri or tetra), solvates or prodrugs. Preparation of specific hydrates or solvates of any compound is a very specialized field and involves their characterization using different techniques such as infrared spectrum, XRD powder diffraction etc. There is no teaching or guidance present in the specification regarding any specific solvents used for preparing specific hydrates or solvates and their characterization using any techniques such as XRD powder diffraction or infrared spectrum etc. There is not even a single example present for preparing any specific hydrate or solvate of instant compounds of formula (I). There is lot of unpredictability regarding stability of different hydrates or solvates of any compound in the art. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of variables R1-R3, A, B, D, E and n and therefore, in absence of such teachings, guidance, presence of working examples and unpredictability, it would require undue experimentation to select specific hydrates or solvates of instant compounds with enhanced stability properties.

In regard to prodrug forms, there is no teaching or guidance present in the specification for preparing specific types of prodrug form such carboxylic acid esters, amino acid or amide esters, phosphate esters, phosphono esters , sulfate esters etc. There is not

even a single working example present in the specification for preparing any type of specific prodrug form of instant compounds of formula (I). There is lot of unpredictability in the art for efficacy of different types of prodrug forms of any known compound following their in vivo administration since their efficacy depends upon various factors such as absorption from gut, metabolism by esterases etc. The instant compounds of formula I encompasses hundreds of thousands of compounds based on the values of variables R1-R3, A, B, D, E and n and therefore, in absence of such teachings, guidance, presence of working examples and unpredictability, it would require undue experimentation to select specific types of prodrug forms of instant compounds of formula (I) which will be effective following in vivo administration.

In regard to enablement rejection of claims 24-29 and 37-43 for using instant compounds for methods of treatment, the specification mentions that the instant compounds are antagonists of NK1, NK2 and NK3 receptors and mentions various in vitro assays for binding these receptors and assessing this antagonism in vivo (see pages 185- 194 of specification). The specification does demonstrate antagonist activity at NK2 receptors in vivo by some representative compounds on page 194. However, there is no teaching in the specification whether some representative compounds encompassed by the instant compounds of formula (I) were actually found to be antagonists at NK1 and NK3 receptors also in these assays. There is no teaching or guidance present in the specification or prior art that hyperactivity of NK1, NK2 and NK3 receptors is implicated in the etiology of every known respiratory disease, allergic disease and urinary incontinence. There is no teaching either in the specification or prior

art references provided to show specific disease conditions which are mediated either by hyperactivity or hypoactivity of NK1, NK2 and NK3 receptors. There is no teaching in the prior art that structurally closely related compounds having antagonist activity at NK2 receptors are well known to have therapeutic utility in treating every known respiratory disease, allergic disease or urinary incontinence. There are no working examples present showing efficacy of instant compounds in known animal models of every known respiratory disease, allergic disease and urinary incontinence. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of variables R1-R3, A, B, D, E and n and therefore, in absence of such teachings, guidance, presence of working examples and prior art, it would require undue experimentation to demonstrate efficacy of instant compounds in known animal models of every known respiratory disease, allergic disease and urinary incontinence and hence their utility for treating these disorders.

In regard to preventing or prophylaxis of any disease condition, it is well known in the art that there are multiple mechanisms involved in the etiology of any known disease condition. Therefore, correcting only one of these several mechanisms (such as antagonism at NK2 receptors in the instant case) will not completely cure or prevent that disease condition.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 24 and 37 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 24 and 37, specific diseases which are mediated specifically by each of NK1, NK2 and NK3 receptors, are not defined.

Allowable Subject Matter

7. Claims 21, 22 and 44-72 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The instant compounds of formula (I) are allowable over the prior art since they are neither disclosed nor obvious over the prior art. In the prior art, Nishi (U.S. Patent 6,511,975, cited on applicant's form 1449) discloses spiropiperidine derivatives which are closely related to instant compounds. However, most closely compounds (see compounds 33-64, 129-160, 225-256 and 321-353 in columns 21-25) disclosed by Nishi differ from the instant compounds in having different value of variable R3 (only H) and furthermore, there is no teaching, suggestion or motivation in the prior art to modify the compounds of Nishi to prepare the instant compounds.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571)272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625